Scientific Abstract

Gene therapy may provide a new therapeutic approach to HIV-1 infection. Our central hypothesis is that a gene encoding RNA molecules which inhibit HIV-1 replication (hammerhead ribozymes: TR/TAT) can be inserted into CD34+ cells (mobilized by G-CSF into the peripheral blood) of subjects with HIV-1 infection; autologous transplantation of the transduced CD34+ cells will lead to production of mature T cells and monocytes which express the hammerhead ribozymes and are thereby resistant to HIV-1 replication. The most direct way to test this hypothesis is with a clinical trial of CD34+ cell transduction, in which the engraftment and survival of cells transduced by a retroviral vector carrying the hammerhead ribozymes (L-TR/TAT-neo) are compared to a frequency of cells transduced by a retroviral vector transduced by a neutral marker vector (LN). The end-points of the trial are 1) determination of the safety of performing the procedure, 2) measurement of the extent and duration of engraftment of transduced cells based upon the presence of the retroviral vector marker and 3) assessment of the relative survival of cells containing the ribozyme vector (L-TR/TAT-neo) compared to cells carrying the neutral vector (LN). This initial trial of gene transfer into CD34+ cells should provide valuable data on the potential efficacy of these techniques and has the possibility of providing subjects with mature hematopoietic and lymphocytic cells which are resistant to HIV-1 replication.